

CLAIMS

What is claimed is:

5 ~~1.~~ An immunomodulatory polynucleotide/microcarrier (IMP/MC) complex, comprising:

 a polynucleotide comprising an immunostimulatory sequence (ISS) linked to a nonbiodegradable microcarrier (MC), wherein the ISS comprises the sequence 5'-C, G-3', with the proviso that if the MC is gold, latex or magnetic, the linkage is other than by biotin/avidin.

10 2. The IMP/MC complex of claim 1, wherein said polynucleotide is covalently linked to said microcarrier.

 3. The IMP/MC complex of claim 1, wherein said polynucleotide is non-covalently linked to said microcarrier.

15 4. The IMP/MC complex of claim 1, wherein said microcarrier is a liquid phase microcarrier.

 5. The IMP/MC complex of claim 1, wherein said microcarrier is a solid phase microcarrier.

 6. The IMP/MC complex of claim 1, wherein said microcarrier is from 10 nm to 10 μ m in size.

20 7. The IMP/MC complex of claim 6, wherein said microcarrier is from 25 nm to 5 μ m in size.

 8. The IMP/MC complex of claim 1, wherein said complex is antigen-free.

 9. The IMP/MC complex of claim 1, wherein the ISS comprises the sequence 5'-T, C, G-3'.

25 10. The IMP/MC complex of claim 1, wherein the ISS comprises the sequence 5'-purine, purine, C, G, pyrimidine, pyrimidine, C, G-3'.

 11. The IMP/MC complex of claim 1, wherein the ISS comprises the sequence SEQ ID NO:1.

12. The IMP/MC complex of claim 9, wherein the ISS comprises the sequence 5'-TCGX₁X₂X₃X₄-3' or the sequence 5'-X₁TCGX₂X₃X₄-3', wherein X₁, X₂, X₃, X₄ are nucleotides.

5 13. The IMP/MC complex of claim 12, wherein the ISS comprises the sequence 5'-TCGTCGX₁-3', wherein X₁ is a nucleotide.

14. The IMP/MC complex of claim 12, wherein the ISS comprises a sequence selected from the group consisting of 5'-TCGTCGA-3', 5'-TCGAAAA-3', 5'-TCGCCCC-3', 5'-TCGGGGG-3' and 5'-TCGTTTT-3'.

10 15. The IMP/MC complex of claim 1, wherein said polynucleotide further comprises the sequence 5'-T, C, G-3'.

16. The IMP/MC complex of any of claims 1, 9, 12, 13, 14 or 15, wherein said complex further comprises an antigen.

17. The IMP/MC complex of claim 16, wherein said antigen is an allergen.

15 18. The IMP/MC complex of claim 1, wherein said polynucleotide comprises a phosphate backbone modification.

19. The IMP/MC complex of claim 18, wherein said phosphate backbone modification is a phosphorothioate.

20 ~~20.~~ An immunomodulatory polynucleotide/microcarrier (IMP/MC) complex, comprising:

20 a polynucleotide linked to a nonbiodegradable microcarrier (MC), wherein the polynucleotide comprises the sequence 5'-C, G-3' and wherein the polynucleotide is 7 nucleotides in length.

21. The IMP/MC complex of claim 20, wherein the polynucleotide comprises the sequence 5'-T, C, G-3'.

25 22. The IMP/MC complex of claim 21, wherein the polynucleotide consists of the sequence 5'-TCGX₁X₂X₃X₄-3' or the sequence 5'-X₁TCGX₂X₃X₄-3', wherein X₁, X₂, X₃, X₄ are nucleotides.

23. The IMP/MC complex of claim 22, wherein the polynucleotide consists of the sequence 5'-TCGTCGX₁-3', wherein X₁ is a nucleotide.

24. The IMP/MC complex of claim 22, wherein the polynucleotide consists of a sequence selected from the group consisting of 5'-TCGTCGA-3', 5'-TCGAAAA-3', 5'-TCGCCCC-3', 5'-TCGGGGG-3' and 5'-TCGTTTT-3'.

5 25. The IMP/MC complex of claim 20, wherein said polynucleotide further comprises the sequence 5'-T, C, G-3'.

26. The IMP/MC complex of claim 20, wherein said complex further comprises an antigen.

27. The IMP/MC complex of claim 26, wherein said antigen is an allergen.

10 28. The IMP/MC complex of claim 20, wherein said polynucleotide comprises a phosphate backbone modification.

29. The IMP/MC complex of claim 28, wherein said phosphate backbone modification is a phosphorothioate.

15 ~~30.~~ A method of modulating an immune response in an individual comprising administering to an individual a composition comprising an immunomodulatory polynucleotide/microcarrier (IMP/MC) complex in an amount sufficient to modulate an immune response in said individual, said complex comprising a polynucleotide linked to a nonbiodegradable microcarrier (MC), wherein the polynucleotide comprises the sequence 5'-C, G-3'.

20 31. The method of claim 30, wherein said microcarrier is a solid phase microcarrier.

32. The method of claim 30, wherein said microcarrier is a liquid phase microcarrier.

33. The method of claim 30, wherein said polynucleotide is covalently linked to said microcarrier.

25 34. The method of claim 30, wherein said polynucleotide is non-covalently linked to said microcarrier.

35. The method of claim 30, wherein said microcarrier is less than about 10 μm in size.

36. The method of claim 30, wherein said complex is antigen-free.

37. The method of claim 30, wherein a Th1-type immune response is stimulated.

38. The method of claim 30, wherein a Th2-type immune response is suppressed.

5 39. The method of claim 30, wherein interferon-gamma (IFN- γ) is increased in said individual.

40. The method of claim 39, wherein said individual has idiopathic pulmonary fibrosis.

10 41. The method of claim 30, wherein interferon-alpha (IFN- α) is increased in said individual.

42. The method of claim 41, wherein said individual has a viral infection.

43. The method of claim 30, wherein levels of IgE is reduced in said individual.

15 44. The method of claim 30, wherein the polynucleotide comprises the sequence 5'-T, C, G-3'.

45. The method of claim 30, wherein the polynucleotide comprises the sequence 5'-purine, purine, C, G, pyrimidine, pyrimidine, C, G-3'.

46. The method of claim 44, wherein the polynucleotide comprises the sequence SEQ ID NO:1.

20 47. The method of claim 44, wherein the polynucleotide comprises the sequence 5'-TCGX₁X₂X₃X₄-3' or the sequence 5'-X₁TCGX₂X₃X₄-3', wherein X₁, X₂, X₃, X₄ are nucleotides.

48. The method of claim 47, wherein the polynucleotide comprises the sequence 5'-TCGTCGX₁-3', wherein X₁ is a nucleotide.

25 49. The method of claim 47, wherein the polynucleotide comprises a sequence selected from the group consisting of 5'-TCGTCGA-3', 5'-TCGAAAA-3', 5'-TCGCCCC-3', 5'-TCGGGGG-3' and 5'-TCGTTTT-3'.

50. The method of claim 30, wherein said polynucleotide further comprises the sequence 5'-T, C, G-3'.

51. The method of any of claims 30, 44, 47, 48, 49 or 50, wherein said polynucleotide is 7 nucleotides in length.

52. The method of any of claims 30, 44, 47, 48, 49 or 50, wherein said composition further comprises an antigen.

5 53. The method of claim 52, wherein said antigen is an allergen.

54. The method of claim 30, wherein said polynucleotide comprises a phosphate backbone modification.

~~55. The method of claim 54, wherein said phosphate backbone modification is a phosphorothioate.~~

10 ~~56.~~ A kit, comprising:

an immunomodulatory polynucleotide/microcarrier (IMP/MC) complex, said complex comprising a polynucleotide linked to a nonbiodegradable microcarrier (MC), wherein said polynucleotide comprises the sequence 5'-C, G-3'; and

15 optionally, instructions for use of IMP/MC complex in immunomodulation of an individual.

57. The kit of claim 56, wherein said polynucleotide is covalently linked to said microcarrier.

58. The kit of claim 56, wherein said polynucleotide is non-covalently linked to said microcarrier.

20 59. The kit of claim 56, wherein said microcarrier is a liquid phase microcarrier.

60. The kit of claim 56, wherein said microcarrier is a solid phase microcarrier.

25 61. The kit of claim 56, wherein said microcarrier is from 10 nm to 10 μ m in size.

62. The kit of claim 61, wherein said microcarrier is from 25 nm to 5 μ m in size.

63. The kit of claim 56, wherein said complex is antigen-free.

30 64. The kit of claim 56, wherein the polynucleotide comprises the sequence 5'-T, C, G-3'.

65. The kit of claim 56, wherein the polynucleotide comprises the sequence 5'-purine, purine, C, G, pyrimidine, pyrimidine, C, G-3'.

66. The kit of claim 64, wherein the ISS comprises the sequence SEQ ID NO:1.

5 67. The kit of claim 64, wherein the polynucleotide comprises the sequence 5'-TCGX₁X₂X₃X₄-3' or the sequence 5'-X₁TCGX₂X₃X₄-3', wherein X₁, X₂, X₃, X₄ are nucleotides.

68. The kit of claim 67, wherein the polynucleotide comprises the sequence 5'-TCGTCGX₁-3', wherein X₁ is a nucleotide.

10 69. The kit of claim 67, wherein the polynucleotide comprises a sequence selected from the group consisting of 5'-TCGTCGA-3', 5'-TCGAAAA-3', 5'-TCGCCCC-3', 5'-TCGGGGG-3' and 5'-TCGTTTT-3'.

70. The kit of claim 56, wherein said polynucleotide further comprises the sequence 5'-T, C, G-3'.

15 71. The kit of any of claims 56, 64, 67, 68, 69 or 70, further comprising an antigen.

72. The kit of claim 71, wherein said antigen is an allergen.

73. The kit of claim 56, wherein said polynucleotide comprises a phosphate backbone modification.

20 74. The kit of claim 73, wherein said phosphate backbone modification is a phosphorothioate.

75. A kit, comprising:
the IMP/MC complex of any of claims 20-24.

25 76. A composition comprising the IMP/MC complex of claim 1 or claim 20 and a pharmaceutically acceptable excipient.

77. A composition according to claim 76, wherein the composition is antigen-free.

78. A composition according to claim 76, wherein the composition further comprises an antigen.

30 79. A composition according to claim 78, wherein the antigen is an allergen.